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Diabetes Mellitus

A Review of Some Recent Investigations into the Nature Of the Clinical Syndrome

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THE CONCEPT that diabetes mellitus results from insulin deficiency is based upon the observation that in dogs removal of the pancreas was followed by hyperglycemia, glycosuria, ketosis and death,[63] and that the administration of insulin, in the form of pancreatic extract, could prevent these sequelae.[7] In the 41 years that have elapsed since the original communication of Banting and Best rapid advances have been made in both the clinical and the biochemical aspects of diabetes, and diabetic ketoacidosis has been virtually eliminated as a cause of death.

On the other hand, although the average life span of a patient subsequent to the diagnosis of diabetes has increased from six to 18 years since the advent of insulin,[38] the degenerative changes historically associated with diabetes have not been prevented. It has been estimated that these lesions account for approximately 80 per cent of deaths among patients with diabetes as compared with 30 per cent in the general population.[11] Considerable heat and energy have been dissipated over the controversy of whether or not careful control of hyperglycemia can affect the development of the "vascular complications" of diabetes, and these issues still remain unsettled. However, there would appear to be little question that premature atherosclerosis, nephropathy, neuropathy and retinopathy still occur quite frequently in patients with diabetes.

In most recent years clinical investigation of diabetes mellitus has tended to become focused more and more on the two following questions:

1. Is diabetes a simple deficiency disease, characterized by the absence of sufficient insulin to maintain glucose homeostasis, in which generalized angiopathy may develop as a result of the abnormal carbohydrate metabolism?

2. Can diabetes be diagnosed before the development of clinical manifestations of abnormal carbohydrate metabolism, and if so, can anything be done to forestall its clinical progression?

In the following review, we will attempt to summarize and evaluate some recent investigations that bear on these two questions. An attempt will be made to be selective, and the subject matter to be presented will depend to a considerable extent on the areas of investigation that hold the most interest for us. Several excellent books have recently appeared which provide comprehensive reviews of all aspects of diabetes.[25,70]

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For information on preparation of manuscript, see advertising page 2

EDITORIAL

Sulfonamide-Resistant Meningococci

EVER SINCE the early observations regarding the effectiveness of sulfonamides in the treatment and prophylaxis of meningococcus infections, these drugs have been regarded as the first and unfailing recourse in this disease. Some authorities have recommended the use, additionally, of penicillin, in case some strains might be resistant to sulfonamides —usually with the comment that resistant strains had escaped detection.

Recently Millar et al (J.A.M.A. 186:139, Oct. 12, 1963) reported the isolation of strains of meningococci which were resistant to sulfonamides and did not respond adequately to treatment with these drugs. Failures have been noted, especially in mass prophylaxis, with diminished effect in the reduction of carriers. Thus far, these results have not been encountered commonly in civilian populations but have occurred in military personnel, among whom chemoprophylaxis has been employed extensively.

Conceivably the use of mass prophylaxis may have been the very mechanism by which the emergence of resistant strains has been induced.

A disturbing possibility is that this information may lead clinicians to abandon the use of sulfadiazine and sulfasoxizole (Gantrisin®) completely and to rely on the use of penicillin alone in the treatment of these highly fatal and fulminant infections. Some strains of meningococci are resistant to penicillin. In a number of instances, some of which are a matter of my personal knowledge, the employment of the usual dosage of procaine penicillin in the treatment of unexplained fever has been followed in two or three days by progressive meningococcus disease, sometimes with petechiae and other evidences of meningococcemia.

The course of meningococcus disease does not usually provide, on the basis of sensitivity tests, the opportunity to determine the most appropriate drug for treatment. The diagnosis can be established often on immediate evidences which are as definitive as the results of bacteriological culture (petechial rash, profound toxemia, direct smears from petechial puncture or from the spinal fluid). The choice of an antimicrobial agent, thus, must be a matter of clinical empiricism, the agents most likely to be successful being promptly employed.

These infections constitute medical emergencies. Death or serious damage may result in a very few hours. There is no reason to debate the single best antibacterial agent; it is preferable to select a combination of drugs which can be given promptly with some assurance of success. Treatment usually should be by the intravenous route and, providing that reasonably generous amounts of intravenous fluid are given along with the therapeutic agent, medication is devoid of risks which are disproportionate to the mounting danger of the disease.

In the light of present knowledge, it would seem appropriate not to abandon sulfonamide therapy but to combine this with the use of penicillin. The use of procaine penicillin in doses of 300,000 to 600,000 units is inadequate: Along with adequate intravenous dosage of sodium sulfadiazine or sulfasoxizole (5 to 6 gm over a 24-hour period for adults), aqueous penicillin G in dosage of 20 million units in 24 hours should be given by continuous drip. Similar dosage should be continued for the next week, and then be gradually reduced in the ensuing few days.

EDWARD B. SHAW, M.D.

C.M.A.'s Audio-Digest— A Decade of Progress

IT HAS BEEN a full decade now since the House of Delegates of the C.M.A. adopted a local, small-scale experiment in continuing postgraduate medical education. The experiment's name: The Audio-Digest Foundation. Its avowed purposes: To provide the practicing physician with a convenient mode of continuing home and office postgraduate